INFLUENCE OF AGE AND SEX ON THE PHARMACOKINETICS OF THIOPENTONE

J. H. CHRISTENSEN, F. ANDREASEN AND J. A. JANSEN

SUMMARY

Thiopentone was given to eight women and eight men (60–79 yr). The disappearance of thiopentone from the venous blood was described by a three-compartment open model. The only significant difference between the sexes was a higher initial venous concentration in males. The dose (mg kg$^{-1}$) for induction was 70% of the value ($P < 0.05$) previously reported for a comparable group of younger men and women (20–40 yr). The volumes of distribution $V_2$ and $V_3$ were larger in the elderly ($P < 0.05$). The terminal half-lives were increased with advancing age (from 75% to 100% on average) ($P \leq 0.01$). The clearance value was 50% greater in the older women than in a group of young women. For all groups a significant correlation between initial drug concentration and $k_2$ supported the hypothesis that the redistribution rate constant $k_{12}$ is the predominant factor in the pharmacokinetic profile of a dose of thiopentone sufficient to obtund the eyelash reflex.

The dose of thiopentone required to induce anaesthesia depends on the age and the sex of the patient, Dundee (1954) and Christensen and Andreasen (1978) demonstrating that anaesthesia was induced with smaller doses in the elderly. The average induction dose (mg kg$^{-1}$) was significantly less in women than in men when all age groups were considered but no significant differences were present when groups of different sex but similar ages were compared (Christensen and Andreasen, 1978). Recently, the pharmacokinetics of thiopentone were compared in young men and women after the administration of the dose required to induce anaesthesia (Christensen, Andreasen and Jansen, 1980). A larger $V_3$ and a longer $t_{1/2}$ were noted in the women. The results suggested that the rate constant $k_{12}$, rather than the initial volume of distribution, was the determinant of the dose necessary to obtund the eyelash reflex.

The pharmacokinetics of thiopentone in the elderly have not been described. The present study allowed comparison of the findings with the results obtained in our previous study (Christensen, Andreasen and Jansen, 1980). The objectives were: (1) to compare groups of elderly men and women with respect to dose and pharmacokinetics; (2) to establish a basis for the comparison of four groups: young women, young men, elderly women and elderly men.

PATIENTS AND METHODS

Eight female and eight male patients gave informed consent to the study. The age range was 60–79 yr. The women underwent minor gynaecological operations, the men orthopaedic procedures. The diseases were not of an acute nature and no patients had evidence of a disease other than that for which surgery was indicated.

Pethidine 0.8 mg kg$^{-1}$ and atropine 0.5 mg were given i.m. 30–60 min before the induction of anaesthesia. The thiopentone solution (Leopental, 2.5%) was injected to a vein on the back of the hand until the eyelash reflex was obtunded. The first 200 mg was given over 25 s. After that repeated doses of 50 mg were injected over 2 s every 20 s. Before each injection the patient was examined to determine the presence or absence of the eyelash reflex. Suxamethonium 100 mg was given to facilitate tracheal intubation and anaesthesia was maintained with halothane in nitrous oxide in oxygen. The lungs were ventilated artificially and every anaesthetic was administered by the same anaesthetist (J. H. C.).

Blood samples for the determination of thiopentone were withdrawn from an indwelling catheter inserted to a large cubital vein in the arm opposite that used for the injection. A control
sample was taken before induction. The first sample was drawn 40 s after the last injection of thiopentone. Further samples were taken at 5, 15, 30, 45, 60 and 90 min and 2, 3, 4, 6, 8, 12, 22–24 h. The blood was allowed to coagulate, serum was obtained by centrifugation and kept refrigerated for a few days until it was analysed.

Thiopentone was analysed by high performance liquid chromatography (Christensen and Andreasen, 1979). The sensitivity of the method was 0.05 μg ml⁻¹.

Calculation of pharmacokinetic data

A three-compartment open model with elimination from the central compartment only was used to describe the disappearance of thiopentone from the serum. The model has been described in detail previously (Christensen, Andreasen and Jansen, 1980). The symbols for the compartmental model are in accordance with the guidelines suggested in this Journal (Editorial, 1979).

Statistical calculations

The statistical significance of observed differences was tested by the Mann-Whitney test. Correlations were tested by standard t statistics.

RESULTS

The average doses necessary for the induction of anaesthesia are listed in table I. The men required a greater dose than the women but in relation to body weight the doses were equal. On the other hand, the concentration in the peripheral venous blood was significantly greater in the male patients. For all 16 patients there was a correlation between the dose in mg per kg body weight and the initial venous concentration (P<0.05).

The relationship between venous serum concentration and time is shown in figure 1 for one female and one male patient. A three-compartment open model with elimination from the central compartment only can describe both curves and the same was true for the other 14 patients. The pharmacokinetic parameters are shown in table II (women) and in table III (men). The volumes of distribution, the rate constants, the half-lives and the clearances showed no significant differences in the two groups.

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Induction dose</td>
<td>231±25.8</td>
<td>312±44.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(mg kg⁻¹)</td>
<td>3.90±0.68</td>
<td>3.97±0.76</td>
<td>n.s.</td>
</tr>
<tr>
<td>Venous concn</td>
<td>19.2±6.5</td>
<td>34.3±18.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>(μg ml⁻¹)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TABLE I. The induction dose of thiopentone (mg and mg per kg body weight) and the initial venous concentration in eight elderly women and in eight elderly men (mean ± SD)

![Graph](image-url)  
**Fig. 1.** The serum concentration of thiopentone as a function of time for patient O in table II and for patient ▲ in table III.
Pharmacokinetics of thiopentone

The methodology of the present study of elderly men and women was similar to that in our study of young men and women (Christensen, Andreasen and Jansen, 1980) and allows comparisons: elderly men and women (\( \geq 60 \) yr) v. younger men and women (20–40 yr). For all 32 patients the elimination of thiopentone from serum could be described by a three-compartment open model (Christensen, Andreasen and Jansen, 1980).

Tables V-XI list differences of statistical significance between the four groups of patients.

### Influence of sex

For younger patients the dose necessary for induction was significantly greater in the men; the same was true for the elderly patients (table V). If the doses were corrected for differences in body weight, men and women required the same dose. This was found for both age groups (table VI). This finding is in accord with our initial study in which the doses of thiopentone required to induce

### Discussion

The methodology of the present study of elderly men and women was similar to that in our study of young men and women (Christensen, Andreasen and Jansen, 1980) and allows comparisons: elderly men and women (\( \geq 60 \) yr) v. younger men and women (20–40 yr). For all 32 patients the elimination of thiopentone from serum could be described by a three-compartment open model (Christensen, Andreasen and Jansen, 1980).

### Influence of sex

For younger patients the dose necessary for induction was significantly greater in the men; the same was true for the elderly patients (table V). If the doses were corrected for differences in body weight, men and women required the same dose. This was found for both age groups (table VI). This finding is in accord with our initial study in which the doses of thiopentone required to induce

### Table II. Pharmacokinetic parameters of thiopentone in eight elderly women. The data are calculated from the concentrations in venous blood after i.v. administration within 2 min of an induction dose (250–400 mg)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Weight (kg)</th>
<th>( V_1 ) (litre)</th>
<th>( V_2 ) (litre)</th>
<th>( V_3 ) (litre)</th>
<th>( k_{12} ) (min(^{-1}))</th>
<th>( k_{13} ) (min(^{-1}))</th>
<th>( k_{10} ) (min(^{-1}))</th>
<th>( T_{1/2}^a ) (min)</th>
<th>( T_{1/2}^b ) (min)</th>
<th>CI (litre min(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>□</td>
<td>72</td>
<td>19.9</td>
<td>15.6</td>
<td>111.5</td>
<td>0.031</td>
<td>0.015</td>
<td>0.0085</td>
<td>8.3</td>
<td>54</td>
<td>813</td>
</tr>
<tr>
<td>■</td>
<td>66</td>
<td>18.4</td>
<td>36.4</td>
<td>337.2</td>
<td>0.055</td>
<td>0.028</td>
<td>0.0081</td>
<td>6.3</td>
<td>69</td>
<td>2223</td>
</tr>
<tr>
<td>○</td>
<td>61</td>
<td>4.5</td>
<td>19.0</td>
<td>112.4</td>
<td>0.540</td>
<td>0.085</td>
<td>0.0481</td>
<td>8.9</td>
<td>29</td>
<td>616</td>
</tr>
<tr>
<td>●</td>
<td>54</td>
<td>7.7</td>
<td>10.6</td>
<td>83.3</td>
<td>0.099</td>
<td>0.042</td>
<td>0.0179</td>
<td>3.3</td>
<td>30</td>
<td>668</td>
</tr>
<tr>
<td>△</td>
<td>47</td>
<td>16.9</td>
<td>19.0</td>
<td>91.7</td>
<td>0.043</td>
<td>0.015</td>
<td>0.0113</td>
<td>7.0</td>
<td>58</td>
<td>662</td>
</tr>
<tr>
<td>▲</td>
<td>63</td>
<td>10.3</td>
<td>20.0</td>
<td>213.7</td>
<td>0.117</td>
<td>0.054</td>
<td>0.0261</td>
<td>2.9</td>
<td>32</td>
<td>875</td>
</tr>
<tr>
<td>▼</td>
<td>58</td>
<td>8.5</td>
<td>20.1</td>
<td>132.6</td>
<td>0.210</td>
<td>0.047</td>
<td>0.0262</td>
<td>2.0</td>
<td>35</td>
<td>706</td>
</tr>
<tr>
<td>▼</td>
<td>60</td>
<td>18.1</td>
<td>26.6</td>
<td>208.2</td>
<td>0.041</td>
<td>0.023</td>
<td>0.0090</td>
<td>7.5</td>
<td>64</td>
<td>1354</td>
</tr>
</tbody>
</table>

### Table III. Pharmacokinetic parameters of thiopentone in eight elderly men. The data are calculated from the concentrations in venous blood after i.v. administration within 2 min of an induction dose (250–400 mg)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Weight (kg)</th>
<th>( V_1 ) (litre)</th>
<th>( V_2 ) (litre)</th>
<th>( V_3 ) (litre)</th>
<th>( k_{12} ) (min(^{-1}))</th>
<th>( k_{13} ) (min(^{-1}))</th>
<th>( k_{10} ) (min(^{-1}))</th>
<th>( T_{1/2}^a ) (min)</th>
<th>( T_{1/2}^b ) (min)</th>
<th>CI (litre min(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>□</td>
<td>79</td>
<td>12.3</td>
<td>29.1</td>
<td>125.3</td>
<td>0.050</td>
<td>0.021</td>
<td>0.017</td>
<td>7.3</td>
<td>94</td>
<td>984</td>
</tr>
<tr>
<td>■</td>
<td>97</td>
<td>14.1</td>
<td>29.9</td>
<td>152.0</td>
<td>0.079</td>
<td>0.032</td>
<td>0.016</td>
<td>4.5</td>
<td>52</td>
<td>798</td>
</tr>
<tr>
<td>○</td>
<td>75</td>
<td>6.0</td>
<td>15.0</td>
<td>118.1</td>
<td>0.085</td>
<td>0.047</td>
<td>0.046</td>
<td>3.5</td>
<td>41</td>
<td>612</td>
</tr>
<tr>
<td>●</td>
<td>86</td>
<td>4.5</td>
<td>29.5</td>
<td>69.6</td>
<td>0.214</td>
<td>0.053</td>
<td>0.036</td>
<td>2.1</td>
<td>65</td>
<td>590</td>
</tr>
<tr>
<td>△</td>
<td>73</td>
<td>16.9</td>
<td>47.7</td>
<td>282.8</td>
<td>0.098</td>
<td>0.017</td>
<td>0.015</td>
<td>4.4</td>
<td>94</td>
<td>1580</td>
</tr>
<tr>
<td>▲</td>
<td>68</td>
<td>3.3</td>
<td>17.6</td>
<td>60.1</td>
<td>0.230</td>
<td>0.068</td>
<td>0.054</td>
<td>1.8</td>
<td>45</td>
<td>470</td>
</tr>
<tr>
<td>▼</td>
<td>76</td>
<td>9.1</td>
<td>22.8</td>
<td>103.3</td>
<td>0.067</td>
<td>0.029</td>
<td>0.016</td>
<td>4.4</td>
<td>61</td>
<td>857</td>
</tr>
<tr>
<td>▼</td>
<td>83</td>
<td>11.8</td>
<td>35.0</td>
<td>86.9</td>
<td>0.299</td>
<td>0.025</td>
<td>0.028</td>
<td>1.8</td>
<td>51</td>
<td>440</td>
</tr>
</tbody>
</table>

### Table IV. Statistical significance of the relationship between the rate constant \( k_{12} \) and the venous serum concentration at the moment of onset of sleep in elderly men and women

<table>
<thead>
<tr>
<th></th>
<th>( n )</th>
<th>( r )</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>8</td>
<td>0.92</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>0.81</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Men</td>
<td>8</td>
<td>0.38</td>
<td>n.s.</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>0.78</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

### Table V. Average induction dose of thiopentone (mg ± SD) in young and elderly patients (eight patients in each of four groups)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Women</th>
<th>Men</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–40 yr</td>
<td>319 ± 37</td>
<td>388 ± 52</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>60–79 yr</td>
<td>231 ± 25.8</td>
<td>312 ± 44.3</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>
anaesthesia were compared in 540 patients studied over a 3-week period in our hospital (Christensen and Andreasen, 1978).

The concentration of thiopentone 20 s after the disappearance of the ciliary reflex was greater when the young men were compared with the young women, but the difference was not statistically significant. In the elderly the difference between the sexes was statistically significant (table VII). Thus, the distribution after administration of the same dose in mg per kg body weight differed between men and women. A relatively large apparent initial distribution volume in the women may reflect accumulation in certain more accessible tissues in the women than in the men. How this initial distribution pattern influences the effect is not clear. Calculations concerning the disposition of thiopentone to different tissues have been performed by Price and colleagues (1960) and by Bischoff and Dedrick (1968). A relatively rapid increase in the amount of the drug was found in the viscera (central nervous system, myocardium, kidneys, portal circulation). However, no attempt was made by these authors to distinguish between men and women.

Average volumes of distribution are shown in tables VIII and IX. $V_1$, which is not shown, was about 30% greater in the elderly women than in the elderly men (n.s.) and 20% greater in the young women as compared with the young men. $V_3$ was almost three times as great in the young women as in the young men ($P<0.05$). In the elderly the difference was not significant. The values of $V_2$ do not show any significant differences. The elimination half-lives (table X) are shorter in the men, but only the differences between the two young groups are significant. For the plasma clearance none of the differences indicating a larger value for the men was significant (table XI).

### Table VI. Average induction dose of thiopentone (mg per kg body weight ± SD) in young and elderly patients

<table>
<thead>
<tr>
<th></th>
<th>20-40 yr</th>
<th>60-79 yr</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>5.43 ± 0.64</td>
<td>3.90 ± 0.68</td>
<td>P &lt; 0.01</td>
</tr>
<tr>
<td>Men</td>
<td>5.25 ± 1.05</td>
<td>3.97 ± 0.76</td>
<td>P &lt; 0.05</td>
</tr>
</tbody>
</table>

### Table VII. The venous concentration (µg ml⁻¹) of thiopentone at the moment of onset of sleep (mean ± SD) in young and elderly patients

<table>
<thead>
<tr>
<th></th>
<th>20-40 yr</th>
<th>60-79 yr</th>
<th>n.s.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>38.6 ± 24.1</td>
<td>19.2 ± 6.5</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>49.8 ± 19.7</td>
<td>34.3 ± 18.4</td>
<td></td>
</tr>
</tbody>
</table>

### Table VIII. $V_2$ (litre) in young and elderly patients (mean with ranges)

<table>
<thead>
<tr>
<th></th>
<th>20-40 yr</th>
<th>60-79 yr</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>12.4</td>
<td>20.9</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Men</td>
<td>12.6</td>
<td>28.3</td>
<td>P &lt; 0.05</td>
</tr>
</tbody>
</table>

### Table IX. $V_3$ (litre) in young and elderly patients (mean with ranges)

<table>
<thead>
<tr>
<th></th>
<th>20-40 yr</th>
<th>60-79 yr</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>92.8</td>
<td>161.3</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Men</td>
<td>31.6</td>
<td>125.0</td>
<td>P &lt; 0.01</td>
</tr>
</tbody>
</table>

### Table X. $T_1^\beta$ (min) in young and elderly patients (mean with ranges)

<table>
<thead>
<tr>
<th></th>
<th>20-40 yr</th>
<th>60-79 yr</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>535</td>
<td>990</td>
<td>P = 0.01</td>
</tr>
<tr>
<td>Men</td>
<td>327</td>
<td>791</td>
<td>P &lt; 0.01</td>
</tr>
</tbody>
</table>

### Table XI. Clearance (litre min⁻¹) in young and elderly patients (mean with ranges)

<table>
<thead>
<tr>
<th></th>
<th>20-40 yr</th>
<th>60-79 yr</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>0.131</td>
<td>0.190</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Men</td>
<td>0.164</td>
<td>0.220</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

### Influence of age

Significant decreases in induction dose in mg and in mg per kg body weight were seen with
advancing age (tables V and VI); the decrease was about 25%. The findings are in accord with our previous study (Christensen and Andreasen, 1978) and with the results of Dundee (1954). Although the average venous serum concentration (table VII) seems considerably less in the elderly patients the differences are not statistically significant. The volumes of distribution became larger with increasing age. A 32–45% increase in $V_1$ was not significant, but $V_2$ and $V_3$ were significantly increased in the elderly patients (tables VIII and IX). $V_3$ in elderly men was increased almost fourfold. The average weight of the young men was 76 kg compared with 80 kg for the elderly. The two age groups of women had similar average body weight (young 59 kg and elderly 60 kg). It should be noted that Novak (1972) reported that body fat increased from 18 to 36% of the body weight when males of 18–25 yr of age were compared with males from 65–85 yr. In the same age groups he found an increase in women from 33 to 45%. An increased volume of distribution with advancing age has been found for diazepam ($V_{74}^a$) (Klotz et al., 1975). No significant change with age was found for the distribution volumes of paracetamol, phenylbutazone, warfarin or sulphamethizole (Crooks, O'Malley and Stevenson, 1976). The terminal half-life of thiopentone (table X) was significantly increased with advancing age in both sex groups. Antipyrine (O'Malley et al., 1971; O'Malley, 1973; Vestal et al., 1975) and paracetamol (Briant et al., 1975; Triggs et al., 1975) have a prolonged $T_1$ in elderly patients. Diazepam (Klotz et al., 1975) and chlormethiazole (Nation et al., 1976) have significantly prolonged half-lives in elderly patients.

A higher clearance was found for thiopentone with advancing age in both women and men (table XI), but the difference was statistically significant only in the women. An increased clearance with advancing age was found for phenytoin in people older than 65 yr compared with people less than 45 yr by Hayes, Langman and Short (1975). A decreased binding of phenytoin was correlated with this increase in clearance. We (unpublished observations) have found a decrease in the binding of thiopentone to serum proteins in elderly patients.

In connection with our finding of prolonged $T_1$,
larger volumes of distribution and a higher clear-
ance for thiopentone with advancing age, it is
interesting that the clearance of diazepam was
found to be unchanged in elderly patients while $V^\text{ss}$
was increased and the half-life was prolonged
dependently (Klotz et al., 1975).

Figure 2 shows the relationship between the
initial venous concentration and $k_{12}$ for 31
patients. The relationship confirms our previous
finding that the rate constant ($k_{12}$) rather than the
initial volume of distribution determines the dose
necessary for induction.

$k_{12}$ is probably determined by a combination of
haemodynamic and diffusion parameters. Measurement of the initial arterial concentration
may further contribute to the elucidation of the
dose-concentration-effect relationship.

ACKNOWLEDGEMENT
This study was supported by the Danish Heart Association.

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INFLUENCE DE L'ÂGE ET DU SEXE SUR LA
PHARMACOCINETIQUE DU THIOPENTONE

Resume
On a administre du thiopentone a huit femmes et a huit
hommes ages de 60-79 ans. La disparition du thiopentone du
sang veineux a ete decrete par un modele ouvert a trois
compartiments. La seule difference significative entre les sexes
a ete une plus forte concentration veineuse initiale chez les
hommes. La dose (mg kg$^{-1}$) utilisee pour l'induction a ete de
70% de la valeur ($P<0.05$) signalree precedentement pour un
groupe comparable de femmes et d'hommes plus jeunes (20-40
ans). Les volumes de separation $V_2$ et $V_3$ ont ete plus
importants chez les personnes agees ($P<0.05$). Les demi-vies
terminales ont augmentee avec l'age (de 75% a 100% en
moyenne) ($P<0.01$). La valeur d'elimination a ete de 50% plus
forte chez les femmes agees que dans un groupe de jeunes
femmes. Pour tous les groupes, une correlation significative
entre la concentration initiale de medicament et $k_{12}$ s'outr
l'hypothese que la constante du taux de redistribution $k_{12}$ est le
facteur predominant du profil pharmacoceintique d'une dose de
thiopentone sufisante pour obtenir un reflexe du cil.

EINFLUSS VON ALTER UND GESCHLECHT AUF
DIE PHARMAKOKINETIK VON THIOPENTON

ZUSAMMENFASSUNG
Thiopentone wurde bei acht Frauen und acht Mânnern (60 bis
79 Jahre) verabreicht. Das Ausscheiden des Thiopentons aus
dem Venenblut wurde mittels eines offenen Modells mit drei
Abteilen beschrieben. Den einzig bedeutenden Unterschied
zwischen den Geschlechtern stellte eine hîtere venöse
Anfangskonzentration bei Männern dar. Die Induktionsdosis
(mg kg$^{-1}$) entspricht 70% des Wertes ($P<0.05$), über den
früher bei einer vergleichbaren Gruppe von jüngeren Männern
und Frauen (20 bis 40 Jahre) berichtet wurde. Die Verteilungs-
volumen $V_2$ und $V_3$ wären bei den älteren Patienten grösser
($P<0.05$). Die Terminalhalbwertzeiten wurden mit
zunehmendem Alter gesteigert (von 75% auf 100% im
Durchschnitt) ($P<0.01$). Der Ausscheidungswert war um
50% grösser bei den älteren Frauen als bei einer Gruppe
jüngerer Frauen. Eine bedeutende Korrelation zwischen der
Anfangskonzentration und $k_{12}$ bei allen Gruppen bekräftigte
die Hypothese, dass die Wiederverteilungsgeschwindigkeitskonstante $k_{12}$, der überwiegende Faktor beim pharmakokinetischen Bild einer Thiopentondosis darstellt, die ausreicht, um den Augenwimperreflex zu dämpfen.

INFLUENCIA DE LA EDAD Y DEL SEXO EN LAS FARMACOCINETICAS DE LA TIOPENTONA

SUMARIO
Se administró tiopentona a ocho mujeres y a ocho hombres (de entre 60 y 79 años). La desaparición de la tiopentona de la sangre venosa se describe mediante un modelo abierto de tres compartimentos. La única diferencia significativa entre los sexos fue la de una mayor concentración venosa inicial en los hombres. La dosis (mg kg$^{-1}$) para la inducción fue 70% del valor ($P<0,05$) que se informó anteriormente y que correspondía a un grupo comparativo de mujeres y de hombres más jóvenes (de 20 a 40 años). Los volúmenes de distribución $V_1$ y $V_2$ fueron superiores en los individuos de mayor edad ($P<0,05$). Los periodos de vida media terminales aumentaron a medida que incrementaba la edad (un promedio de entre el 75% y el 100%) ($P<0,01$). El valor correspondiente a la eliminación fue un 50% superior en las mujeres de más edad que en lo relativo a un grupo de mujeres más jóvenes. En lo tocante a todos los grupos, una correlación significativa entre la concentración inicial de la droga y $k_{12}$, respaldó la hipótesis de que la constante del ritmo de redistribución, $k_{12}$, es el factor predominante en lo relativo a la farmacocinética de una dosis de tiopentona que sea suficiente como para anular el reflejo de la pestaña.